UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte JAN G. J. van de WINKEL

Appeal No. 2005-1504
Application No. 09/820,099

ON BRIEF

ELLIS, MILLS and GRIMES, Administrative Patent Judges.

ELLIS, Administrative Patent Judge.

DECISION ON APPEAL[1]

This is an appeal pursuant to 35 U.S.C. § 134 from the examiner's final rejection of claims 1 and 6-12. Claims 2-5 and 13-25 have been cancelled.

Claim 1 is representative of the subject matter on appeal and reads as follows:

1. A method for eliminating a target cell or antigen from the circulatory system of a subject comprising administering to the subject a complex comprising monomeric IgA or a portion thereof that binds to FcαRI, linked to a second portion which specifically binds the target cell or antigen.

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[1]This decision supercedes the one mailed on September 21, 2005.

The references relied upon by the examiner are:

Shen et al. (Shen) WO 98/23646 Jun. 4, 1998

Monteiro et al., "Cellular Distribution, Regulation, and Biochemical Nature of An Fcα Receptor in Humans," J. Exp. Med, vol. 171, pp. 597-613 (March 1990).

Claims 1 and 6-12 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Shen,[2] Monteiro and the teachings of the specification.

Background

Antibodies are part of a class of proteins known as immunoglobulins. Immunoglobulins are produced by the immune system in response to antigens; i.e., substances which are recognized as foreign by the body. Consequently, they are one of the body's most important defenses against disease.

There are five immunoglobulin isotypes- IgG, IgA, IgD, IgM and IgE. IgG is the predominant isotype in human serum, but most of the immunoglobulin-producing cells in the various mucosal and exocrine sites and along the intestinal tract make IgA antibodies. IgA occurs in different molecular forms (monomeric, polymeric and secretory) and subclasses (IgA1 and IgA2). Prior to the present invention, secretory IgA (dimeric IgA) was known to interfere with microbial adherence to epithelial cells in the intestines by forming a coat around the microorganism. According to the specification, "the present invention is based on the discovery that monomeric (serum)

[2] We point out that the author's last name in the publication which both the examiner and the appellant refer to as "Shen" is "Li." That is, the first author's name is Shen Li. Nevertheless, for purposes of consistency, we have also referred to the publication as "Shen."

IgA plays a previously unknown important role in systemic immunity by virtue of its interaction with FcαR [IgA Fc receptor] expressed on Kupffer cells and other FcαR-expressing cells (e.g., neutrophils) present at the interface of the mucosal and systemic immune systems (e.g., the sinusoidal lining of the liver)." Specification, p. 2, lines 20-24.

With respect to the FcαR, the specification discloses that "[a] single class of IgA receptor, FcαRI or CD89, which binds to monomeric IgA" had "been identified and characterized" by prior investigators. Id., p. 1, lines 6-7. It was also known in the art that (I) "FcαRI is constitutively expressed primarily of cytotoxic immune effector cells including monocytes, macrophages, neutrophils, and eosinophils" and that they are "capable of promoting effector cell function" (id., lines 8-10 and 28-29); (ii) "[b]inding of ligand to FcαR triggers phagocytosis and antibody mediated cell cytotoxicity in leukocytes and FcαR-bearing cell lines" (lines 29-30); (iii) "FcαRI binds both antigen-complexed and monomeric (serum) IgAI and IgA2"; and (iv) "[c]ross-linking FcαRI on myeloid effector cells, by polymeric IgA, IgA immune complexes, or mAb specific for epitopes within or outside the ligand binding domain, stimulates degranulation, superoxide release, secretion of inflammatory cytokines, endocytosis and phagocytosis" (line 35 - p. 2, line 4).

As indicated by claim 1, above, the present invention is said to be directed to a method of administering a complex which comprises monomeric IgA, or a portion thereof which binds to the IgA Fc receptor, FcαRI, and a second "portion" which is capable of binding to a target cell or antigen.

Discussion

The examiner argues that Shen discloses (I) "binding agents specific for the FcαR and [that] the binding agents triggers [sic, trigger] an Fc mediated effector cell activity such as phagocytosis"; (ii)"bifunctional binding agents comprising an agent that binds FcαRI and a bacteria . . . or cancer cell or antigen . . . thereof"; (iii) a method of administering the bifunctional agent to a subject intravenously; and (iv) "the binding agents bind the FcαR with the same affinity as a type of IgA which can be monomeric IgA." Answer, p. 3. With respect Monteiro,[3] the examiner argues that the publication evinces that "there is only a single class of IgA Fc receptor, FcαRI, therefore since the agent binds to FcαRI, it would be obvious that the agent would bind to the FcαRI expressed on Kupffer cells. Id., pp. 3-4. The examiner concludes that

> It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to have used the complex comprising monomeric IgA linked to a second antibody (bispecific agent) for the elimination of a target cell or antigen.

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[3] We find that the examiner relies on Monteiro for its disclosure of the presence of the FcαR on Kupffer cells. A method of administering the complex described in claim 1 in Kupffer cells is limited to claim 9. Thus, given our disposition of this case, we need not reach the teachings of this publication.

> One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success to have used the complex comprising monomeric IgA linked to a second antibody (a bispecific agent or multispecific) for the elimination of a target cell or antigen because Shen et al[.] teach FcαRs are capable of interacting with IgA in the form of monomers and binding induces phagocytosis . . . and Shen et al[.] teach that the binding agent binds with the same affinity as monomeric IgA and that the binding agent does not inhibit the binding of IgA [Answer, p. 4].

It is well established that the examiner has the initial burden under 35 U.S.C. § 103 to establish a prima facie case. In re Oetiker, 977 F.2d 1443, 1445, 24 USPQ2d 1443, 1444 (Fed. Cir. 1992); In re Piasecki, 745 F.2d 1468, 1471-72, 223 USPQ 785, 787-88 (Fed. Cir. 1984). To that end, it is the examiner's responsibility to show that some objective teaching or suggestion in the applied prior art, or knowledge generally available in the art, would have led one of ordinary skill in the art to combine the references to arrive at the claimed invention. Pro-Mold & Tool Co. v. Great Lakes Plastics, Inc., 745 F.3d 1568, 1573, 37 USPQ2d 1626, 1629 (Fed. Cir. 1996).

Here, we find that the examiner has not provided any reason based on the applied prior art as to why the claimed invention would have been obvious to one of ordinary skill in the art. That is, if we look only at the subject matter recited in claim 1, we find that it is directed to a method of administering a complex comprising (1) monomeric IgA or a portion thereof which binds to FcαRI; and (2) a portion which specifically binds to a target cell or antigen. We agree with the examiner that Shen teaches a bispecific complex having the second portion; i.e., a complex having a portion which specifically binds to a target cell or antigen (page 1, lines 29-32); however, we do not find that Shen teaches or suggests that the complex comprise monomeric IgA, or a

portion thereof. To the contrary, although Shen recognizes that the receptor for IgA, FcαR, is capable of binding monomeric IgA (p. 3, lines 28-29) and that "[b]inding of IgA to cells bearing these receptors induces a variety of effector functions, such as phagocytosis, antibody dependent cellular cytotoxicity (ADCC), inflammatory mediator release, lysozyme production, and superoxide anion production" (id., lines 29-32); however, Shen teaches using other binding agents whose binding is not blocked by IgA. For example, Shen discloses that "a preferred binding agent binds to a site on an IgA receptor which is different from the binding site for IgA. . . . [such as] monoclonal antibodies specific for different portions of the receptor" [emphases added]. Shen, p. 4, lines 29-33; see also, p. 5, lines 10-12, lines 21-23 and lines 29-34. Shen further discloses that the "preferred binding agents of the invention bind to the FcαR with a higher affinity than a type of IgA" [emphasis added]. Id., p. 6, lines 4-5. Thus, given these and similar teachings found throughout the publication, we agree with the appellant that Shen "teaches away" from using monomeric IgA.

Accordingly, it reasonably follows that we do not find that Shen would have suggested to one of ordinary skill in the art a complex comprising monomeric IgA and a compound which binds to a target cell or antigen. Rather, on this record, the only suggestion we find to administer such a complex is in the appellant's disclosure. Thus, we find that the examiner has engaged in impermissible hindsight to arrive at the conclusion that the claimed invention would have been obvious over Shen and Monteiro. In re Fritch, 972 F.2d 1260, 1266, 23 USPQ2d 1780, 1784 (Fed. Cir. 1992);

Interconnect Planning Corp. v. Feil, 774 F.2d 1132, 1138, 227 USPQ 543, 547 (Fed. Cir. 1985); W.L. Gore & Assocs. v. Garlock, Inc., 721 F.2d 1540, 1553, 220 USPQ 303, 312-313 (Fed. Cir. 1983) cert. denied 469 U.S. 851 (1984)("To imbue one of ordinary skill in the art with knowledge of the invention in suit, when no prior art reference or references of record convey or suggest that knowledge, is to fall victim to the insidious effect of a hindsight syndrome wherein that which only the inventor taught is used against its teacher").

In view of the foregoing, the decision of the examiner is reversed.

Another Issue

Upon return of the application to the corps, the examiner may wish to consider whether the complex recited in claim 1 "reads on" monomeric IgA itself. If so, the examiner should determine whether there is any prior art which teaches a method of administering monomeric IgA to a subject.

REVERSED

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